

REMARKSThe Claim Amendments:

Applicants acknowledge that the Examiner has withdrawn claims 22-33 from consideration. However, applicants have presented claims 22-33 with amendments, where necessary, directed to elected subject matter.

Applicants have amended claims 31-32 to delete the term "N" from the definition of radical X to remove non-elected subject matter therein. As amended, claim 31 is directed to the preparation of compounds of formula I from compounds of formula II and III and claim 32 is directed to the preparation of compounds of formula IIa. Therein, in each formula, radical X is "CH".

None of these amendments adds new matter.

The Rejections:1. 35 U.S.C. §102(b)

Claims 1-14 and 20-21 stand rejected under 35 U.S.C. §102(b) as being anticipated by International PCT Application WO 01/42216 (hereinafter "the '216 application"). The Examiner asserts that the compounds in the '216 application fall within the range of the compounds of the present invention. Specifically, the Examiner points to the '216 compound (e.g., see compound No. 1C-2 at page 16, Table 3, of the '216 application) wherein Y is halogen (F), R² is an alkyl

(methyl), X is carbon, and R³ and R⁴ are hydrogen to support this rejection. Applicants traverse.

Within claim 1 of the present application, applicants recite a proviso that expressly excludes the species of the '216 application cited by the Examiner. Specifically, applicants' proviso recites "provided that when Y is halo, then both, R³ and R⁴, are not simultaneously hydrogen." Thus, the preclusion of hydrogen as a simultaneous embodiment for both radicals R³ and R⁴ in claim 1 and claim 31 renders those claims distinct from the '216 application.

Claims 2-14, 20-21 and 32 depend either directly or indirectly from claims 1 and 31 and therefore they, too, incorporate this limitation. For this reason, claims 2-14, 20-21 and 32, too, are distinct from the '216 application. Accordingly, applicants request that the Examiner withdraw this §102(b) rejection.

2. 35 U.S.C. §103(a)

Claims 1-14 and 20-21 stand rejected under 35 U.S.C. §103(a) as being unpatentable over the '216 application. The Examiner recognizes that the claims of the present invention differ from the '216 application by reciting specific species and a more limited genus than the reference. However, the Examiner asserts that one of skill in the art would, one, expect the species of the present invention to have similar properties to the '216 application species and, two, be motivated to select the presently claimed species from the

genus in the '216 application as a whole. Applicants traverse.

The compounds of the present invention have an unexpected and surprising ability to inhibit apoptosis and/or inhibit IL-1 β release from activated cells (e.g., see specification at page 8, paragraph 18).

It is well established in case law that a compound and its properties are inseparable. See, *In re Papesch*, 315 F.2.d 381 (C.C.P.A. 1963). The courts have "determined the unobviousness and patentability of new chemical compounds by taking into consideration their biological or pharmacological properties." *Id.* at 391. Any structural similarity between a compound sought to be patented and the prior art cannot, *ipso facto*, negate the unobviousness of such a compound.

"And the patentability ... does not depend on the similarity of its formula to that of another compound but of the similarity of the former compound to the latter. There is no basis in law for ignoring any property in making such a comparison." [Emphasis added] *Id.* at 391.

Thus, where, as here, an unexpected property is asserted for a compound, that property must necessarily factor into any patentability calculus, notwithstanding a structural similarity to a compound known in the prior art.

Applicants have demonstrated the unexpectedly better ability of the compounds of the present invention to inhibit apoptosis and/or inhibit IL-1 β release from activated cells. For example, compound example numbers 1 and 2, each, have k_{inact} (measured as $M^{-1}s^{-1}$; rate of enzyme inactivation at a particular inhibitor concentration) of >500000 for inhibition

of Caspases-1, -3 and -8 (listed as range "A", see Table 2, Example 23, pages 74-76 of the specification) except for compound number 1 which has a k_{inact} for Caspase-8 of between 100000 and 500000. Based on the compounds of the '216 application, one of skill in the art would not expect the compounds of the present invention to have such activity.

Thus, the unexpectedly better ability of the compounds of the present invention to inhibit apoptosis renders them unobvious over the '216 application. Accordingly, applicants request that the Examiner withdraw this §103(a) rejection.

Conclusion

Applicants request that the Examiner enter the above amendments, consider the accompanying remarks, and allow the pending claims to pass to issue.

Respectfully submitted,



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